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Regulatory Policy and the Location of Bio-Pharmaceutical FDI in Europe*

Pamina Koenig[†]

Megan MacGarvie[‡]

Abstract

This paper examines the relationship between cross-country differences in drug price regulation and the location of biopharmaceutical Foreign Direct Investment (FDI) in Europe. We use a theoretically-grounded location-choice model and data on 294 investments initiated in 27 European countries between 2002 and 2006 to test the hypothesis that biopharmaceutical companies are less likely to locate new investments in countries with more stringent price regulation.

JEL Codes: F23, I18.

Keywords: pharmaceutical industry, location choices, price regulations, discrete choice model

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1 Introduction

As part of the broader debate over the extent of and reasons for international outward investment, pharmaceutical firms' decisions to invest abroad are at the center of public attention in Europe. The crucial question in this debate is whether rich countries can remain an attractive location for manufacturing firms when confronted with fierce competition from low-wage countries. A frequent response by economists to concerns about such off-shoring is that rich countries have a comparative advantage in high-tech skill-intensive industries, and that outflows of traditional manufacturing will be compensated for by inflows or creation of innovation-based manufacturing plants. The pharmaceutical industry is one example of this type of industry.

The pharmaceutical industry is among the most regulated in the world. Regulation takes the form of strong safety norms with certification processes for drugs, intellectual property rights, and price control mechanisms. Governments justify price regulation as a means to promote equity in access to drugs and reduce costs to national health care systems. However, the enforcement of such regulation measures is complex because of their possible indirect consequences on other aspects of the pharmaceutical market, such as the choice of the country in which companies plan to invest in new production or research facilities. Indeed, several scenarios can be put forward, among which the negative effect of price regulations on firms location decisions. For example, it has been documented that in countries with more stringent price regulations, drug launches are delayed (Danzon 2004; Kyle 2006 and 2007a). In the case the product is first launched in the production country, firms would want to avoid regulated countries. It has been suggested that pharmaceutical firms respond to controversial policy choices by "voting with their feet" in choosing locations. Most recently, Merck was said to be "re-evaluating" its investment in Brazil after that country imposed compulsory licensing on efavirenz, Merck's anti-retroviral AIDS drug. (*The Economist*, May 10 2007, "Brazil's AIDS Program: A conflict of goals").

In this project, we investigate the determinants of the locations of foreign investments in the bio-pharmaceutical sector in 27 European countries between 2002 and 2006. We investigate whether variation in policy regimes across countries helps explain variation in the locations of foreign investments in the pharmaceutical sector.

Our empirical model draws on the literature on location choices in foreign investment. Carlton (1983) was the first paper to use a discrete choice model to study choice of production sites by firms. The subsequent literature analyzed location choices of FDI with the traditional elements of the expected profit in each location, some studies however including a more complete form of demand with the income of contiguous locations (Head, Ries and Swenson, 1999). The new trade theory and the new economic geography literatures provide a foundation for

the empirical analysis of location choices directly issued from theoretical predictions. Head and Mayer (2004) construct a demand variable taking into account the surrounding export destinations as well as the location of competitors, based on the modeling of Krugman (1992). They establish a clear link between the theory of location choice and the predictions derived from their econometric model.

A set of contributions have investigated the influence of public policies on the decision to locate in different countries. Head, Ries and Swenson (1999) study the influence of US states' incentives on the decisions of Japanese affiliates to locate within the United States. Crozet, Mayer and Mucchielli (2004) analyze whether regional policies have an effect on location patterns within France, while Devereux, Griffith and Simpson (2007) apply similar methods to the English case. Those papers end up with mixed evidence of the impact of public policies. In this paper, we present the first evidence of the impact of regulatory constraints on the location choice of affiliates by multinational pharmaceutical firms. In the following, we use the theoretically grounded location-choice model from Head and Mayer (2004) to quantify the role of domestic regulatory policies as an additional determinant of the location choice of pharmaceutical firms.

The paper is structured as follows. Section 2 describes the regulatory policy schemes in the pharmaceutical industry in Europe. Section 3 presents the theoretical model and its empirical implementation. In section 4 we present the investment data, section 5 explains the results and section 6 concludes.

2 Regulatory policy and investment in the pharmaceutical industry

The pharmaceutical industry is perhaps the industry most affected by regulatory choices. Policies concerning the duration and strength of exclusivity awarded by patents are particularly important. The latter policies are essentially consistent across European countries (although the pharmaceutical industry has expressed concern over the enforcement of these rights in some countries), as are policies relating to advertising, wholesale distribution, packaging and labeling of drugs. These homogenized policies are by definition not expected to influence the profitability of the different countries. This is however not the case in the medical sector. As discussed at length by Permanand and Mossialos (2005), "Despite the harmonizing imperative of the SEM, there is still no single European market in medicines." European countries retain control over the pricing of drugs and reimbursement of expenditures. Countries vary in the use of reference pricing, fixed pharmacy profit margins, profit controls for manufacturers, as

well as along other dimensions (see Table 2 of Kyle (2007a)). Countries also vary in their attitudes to parallel trade, or the re-importation of drugs from countries in which prices are lower. All EU countries exert some degree of influence over expenditures on drugs marketed within their boundaries, but individual governments employ different policies. Governments may use formularies (lists of drugs for which patients will be reimbursed), controls on doctors' prescribing behavior, pharmacists, reimbursements of prescription costs, and/or price controls. A common mechanism for controlling prices is to set a price not higher than that of a currently available generic substitute, or to set the price with reference to prices of the same drug in neighboring countries. Some countries (like Spain and the UK) place controls on the profits of pharmaceutical companies. Others, like Denmark, do not control the price charged by the manufacturer, but prohibit price increases after a drug is introduced. Many EU countries also regulate the profit margins of pharmacists. Some countries (like Belgium, France, Spain and the UK) also regulate expenditures on drug marketing.

Our empirical investigation concentrates on the following price regulation policies, which we now define: price controls, reference pricing, therapeutic reference pricing, in each of which price freezes and price cuts can be introduced. Detailed information on the use of these policies in different countries is available in Tables (1) and (2).

Price controls refer to policies that directly control either the manufacturer price or the price reimbursed by the national health service. Reference pricing is a practice in which governments set a maximum reimbursement amount for drug purchases with reference to prices of substitute drugs. Under reference pricing regimes, the price charged by manufacturers is not directly controlled. Danzon (2001) notes that it has typically been used in countries without price controls, and is seen as a less stringent alternative to explicit price controls. However, Danzon notes, "In practice, certain forms of reference pricing can be de facto at least as stringent... particularly for new products." The stringency of reference pricing largely depends on which drugs are used for reference. In some cases, only generic equivalents with the same active ingredient fall into the reference group. In other cases, the reference group consists of any therapeutic substitute on the market, and the drug's prices in other countries are taken into consideration. Most, but not all, countries exempt patented drugs from reference pricing schemes. As Danzon notes, "The decision whether to include on-patent products and to cluster on-patent products with off-patent products raises a critical trade-off between cost control and incentives for R&D, in addition to the issues of therapeutic substitutability." These two forms of price setting for reimbursement will be respectively denoted RP (reference pricing) and TRP (therapeutic reference pricing) in the empirical section of this paper. Germany exempted patented drugs from its reference pricing scheme in 1996. However, in 2004 this exemption was removed, causing the sales of a number of on-patent drugs to fall dramatically. This policy shift was preceded in

2003 by a 16% reduction in reimbursed prices on patented medicines. Denmark expanded the scope of its reference pricing program in 2005, moving from one in which reference pricing was only used when generic equivalents were available to one that incorporates therapeutic equivalents. A similar shift took place in Hungary in 2003 for statins (a class of drugs used to lower cholesterol).

These differences of regulations across countries are likely to be of great concern in the case their application has side-effects for instance on the location of FDI. In theory, all connections between the investment of a firm in country i and the application of policy regulations on drug prices are conceivable.

One could first predict a negative effect of regulations on the investment decision, specifically in situations in which the product is launched in the production country. Firms choose investments locations to maximize profits, which are lower in regulated countries. Firms are also likely to react to countries' policies by choosing to invest elsewhere. Pharmaceutical companies have often threatened to reduce investment in reaction to policy changes. In response to reform proposals in 2002, the Pharma Marketletter reported that the pharmaceutical company Merck KGaA "warned that the reforms could ... influence where it locates a new 300-million euro biopharmaceuticals product plant, its largest-ever investment." Die Welt reported on August 25, 2003 that "the american pharmaceutical firm Pfizer plans to reduce certain activities in Germany following upcoming reforms to the health system. Pfizer has decided to transfer an R&D group from Freiburg, Germany to the United Kingdom. 150 jobs will be affected by this decision." As one of the largest markets in Europe, actions taken by Germany may affect other markets in two ways. Prices for drugs charged in Germany may be factored into other countries' reference pricing calculations, and lower prices in Germany lead to lower prices elsewhere. Secondly, Germany's policy changes may have been viewed by the pharmaceutical industry and other regulators as a test case - if the industry did not react strongly to the change, such changes may have appeared more attractive in other countries. Pharma Marketletter quoted a Merrill Lynch analyst who pointed out the potential snowball effects of Germany's change in policy, asking, "what's to stop France and Italy following guidance from Germany?" ¹.

In the case pharmaceutical firms serve all regional markets, whatever the production country of the drug, one could also model the absence of relationship between price regulations and investments decisions. Finally, a positive impact of regulations on the location of FDI could also be envisioned, if investing firms reach a favorable application of the regulations in the country in which they choose to locate. Evidence on how regulatory policies might influence the decision-making of pharmaceutical firms is given by a number of papers. Kyle (2007a), in a

¹"Govt drug price controls continue to threaten Europe's pharma industry", Pharma Marketletter, December 23, 2002

detailed analysis of international drug launch strategies, shows that drug launches are delayed in countries with price controls. With a focus on developing countries, Lanjouw (2005) shows that drugs are launched earlier in countries with stronger enforcement of Intellectual Property Rights (IPRs). On the other side, Ahlering (2004), in a study of the relationship between regulatory and policy variables in a particular country and the share of a pharmaceutical company's employment in that country, finds little relationship between employment in a country and such factors as intellectual property protection (using the Ginarte-Park index to measure the strength of IP), drug approval times, corporate tax rates, and R&D incentives. Ahlering does, however, find evidence of a positive relationship between the number of price control mechanisms in a country and the share of a company's employment in that country.

Changes like those that took place in Germany are a key element of this study. Most countries do not change their regulatory policies during the time frame of our sample. For example, all of the countries with explicit price controls in our sample maintain these controls throughout the time frame. As a result, it may be difficult to separate the effects of these invariant policy choices from unobserved, invariant characteristics of the country. However, countries that change their policies during the sample period provide an opportunity to examine investment patterns before and after the change. The change in Germany's reference pricing scheme is one such opportunity. Other changes to reference pricing schemes during our period took place in Denmark, Hungary, Spain, and Portugal. Additional variation in the drug price policy environment can be obtained from price freezes that were instituted in several countries during our period. Tables (3) and (4) lists all the policy changes relevant to this paper².

3 The model and the empirical strategy

Following Head and Mayer (2004), we sketch a monopolistic competition trade model à la Dixit and Stiglitz (1977). This model allows to derive a linear-in-logs estimable equation relating the profitability in a potential location to the main determinants of FDI for the pharmaceutical industry. Consider firms from the pharmaceutical industry, located in country i . Each firm produces one variety, which is in our case associated to a particular pharmaceutical product. Demand for a pharmaceutical product produced in country i from a consumer in country j is expressed as

²An increasingly important and controversial factor in the pricing of drugs in the EU is parallel trade, or the re-export of drugs from low-price countries (like Spain, Portugal and Greece). While parallel trade has the potential to lead to price compression within the EU (and has been found to do so in non-drug markets), Kyle (2007b) shows that in fact parallel trade has had little impact on drug prices, due in part to strategic responses by pharmaceutical companies.

$$q_{ij} = \frac{p_{ij}^{-\sigma}}{\sum_{r=1}^R n_r p_{rj}^{1-\sigma}} Y_j, \quad (1)$$

where Y_j is the pharmaceutical consumption in country j , p_{ij} is the delivered price of the pharmaceutical product produced in i and consumed in j , and $\sigma > 1$. The delivered price is the factory price p_i in the home country multiplied by the unit trade cost τ_{ij} . We assume that trade costs comprise all distance and time-related costs of transporting goods.

We want to write the profit that a firm choosing to locate in country r would earn. Firms maximize profits and fix a resulting factory price that is a very simple expression over marginal cost: $p_r = \frac{\sigma}{\sigma-1} c_r$, with c_r being the marginal cost in country r .

Incorporating the equilibrium price in the demand equation, we obtain the quantity that a firm producing in i would ship to each destination j :

$$q_{ij} = \frac{\sigma-1}{\sigma} \frac{(c_i \tau_{ij})^{-\sigma}}{\sum_{r=1}^R n_r (c_r \tau_{rj})^{1-\sigma}} Y_j, \quad (2)$$

where $G_j = \sum_{r=1}^R n_r (c_r \tau_{rj})^{1-\sigma}$ is the price index in country j . We now replace the equilibrium price and quantity in the gross profit earned in country j , $\pi_{ij} = p_i \tau_{ij} q_{ij} - c_i \tau_{ij} q_{ij} = (p_i - c_i) \tau_{ij} q_{ij}$, to get

$$\pi_{ij} = \frac{(c_i \tau_{ij})^{1-\sigma}}{\sigma G_j} Y_j. \quad (3)$$

The profit earned by selling in country j is naturally an increasing function of the size of demand in j , represented by the consumption Y_j . The firm will get a share of that aggregate demand, which depends on the final price paid by consumers in j (the numerator) and on a measure of its competitors' prices (the denominator). The lower the costs of production (c_i) or transaction costs (τ_{ij}) of the producing firm in i , and the higher the costs of its competitors (high G_j), the higher its operating profit.

The profit earned in a location r where the firm could locate is equal to the sum of operating profits in all markets to which the firm could export from r (including r), minus the fixed cost F necessary to establish a plant in country r , which we assume is invariant across countries.

$$\Pi_r = \frac{(c_r)^{1-\sigma}}{\sigma} \sum_j \frac{(\tau_{rj})^{1-\sigma}}{G_j} Y_j - F \quad (4)$$

Following Head and Mayer (2004), we express the net profit as a function of the Krugman market potential in r , M_r :

$$\Pi_r = \frac{(c_r)^{1-\sigma}}{\sigma} M_r - F \quad (5)$$

where $M_r = \sum_j \frac{(\tau_{rj})^{1-\sigma}}{G_j} Y_j$ is a complete measure of demand from all the surrounding locations, incorporating the presence of trade barriers and the effect of competition. The Krugman market potential applied to the pharmaceutical sector in country r sums the pharmaceutical consumption in all countries importing from r (including r). This sum is weighted by transaction costs between country r and destination countries j , and by an index measuring the degree of competition in each market. The demand addressed to a pharmaceutical firm planning to locate in r is thus increasing with consumption in all importing markets including r . This consumption is, however, reduced by two items: 1) the number of other pharmaceutical firms in each market, and 2) the level of transaction costs between r and each market. This theoretically derived expression appears as the most rigorous measure of demand used in trade and geography models and can be compared to the original Harris (1954) form of market potential, in which trade costs are set equal to the inverse measure of distance and where the competition index is absent ($M_r = \sum_j Y_j/d_{rj}$).

Taking logs, the expression for the profit in r becomes

$$\ln \Pi_r = b + (1 - \sigma) \ln c_r + \ln M_r \quad (6)$$

with $b = -(\ln \sigma + \ln F)$.

We specify the cost as a function of local wages w_r (specified here as the unit labor cost of production, which we observe in the 27 destination countries) and add the local statutory tax rate tax_r , which is also likely to affect location decisions as a determinant of the labor market situation.

The market potential variable is constructed from the estimation of bilateral international trade flows, using the Redding and Venables (2004) method explained in the next section. Governmental regulations of the pharmaceutical market are considered as a destination country specific selling cost, entering the competition index in the denominator of the market potential. Because this is our variable of interest, we isolate it outside the market potential in the estimated equation by including PR , a matrix of dummy variables capturing various price regulations. These dummy variables indicate whether the country 1) controls prices explicitly, 2) employs reference pricing schemes to control the amounts reimbursed, 3) uses therapeutic reference pricing, or 4) has frozen or cut the prices of drugs at a given point in time.

Next, we consider the clustering of research-intensive firms in the same location. We include an agglomeration effect variable, computed as the number of pharmaceutical producers in country r in year t . We hence assume that, controlling for the market potential in country r , and controlling for the competition effect emanating from the presence of competitors in the same industry in country r , the presence of other related firms may be beneficial to a firm

considering choosing r . The positive effect may arise from technological spillovers decreasing the input cost c_r , or decreasing the transaction cost τ_{rj} . Furman et al. (2007) (among others) have documented the tendency of biopharmaceutical firms to locate in places with greater R&D capabilities, and as a result we also include the country's annual R&D spending in the pharmaceutical sector. We denote these spillover-related variables $Spill_r$.

Our database contains information about the origin countries of investing firms. In order to take into account the bilateral cost of investment, we add two final variables to the estimation, measuring distance between the investing and the potential host country ($Dist_{ir}$), and whether these countries share a common language ($Lang_{ir}$).

The profit of a firm i in r can be decomposed into the part observed by the researcher, V_{ir} , and the unobserved aspects of the profit e_{ir} . The unobserved elements refer for example to bilateral factors between the firm and the host country affecting the productivity or the firm's production cost. The form of the observed part is specified in the theoretical model up to the vector of parameters β that we will estimate:

$$V_{ir} = \beta_0 + \beta_1 \ln w_r + \beta_2 \ln tax_r + \beta_3 Dist_{ir} + \beta_4 Lang_{ir} + \beta_5 \ln M_r + \beta'_6 PR + \beta'_7 Spill_r. \quad (7)$$

We assume that firms choose the location yielding the highest profit. With error terms distributed according to an extreme value distribution, the probability that a firm i chooses to invest in country r writes in the following logit form:

$$P_{ir} = \frac{\exp(V_{ir})}{\sum_j \exp(V_{ij})} \quad (8)$$

We thus estimate the determinants of location choices in the pharmaceutical industry using a logit model, on the data that are described in the next section. Following several papers in the location choice literature, we estimate a Conditional Logit model of location choices. This model is particularly well suited to applications in which choices are made based on the observable characteristics of the alternatives. In this case, we model profits as a function of the choice attributes described above and a common set of parameters. Chung and Alcacer (2002) use the Random Parameters Logit model, which allows the effect of location characteristics to vary across investors. While we do not pursue this estimation strategy, we do examine whether different types of investment respond differently to regulation in some specifications.

4 Data

We estimate a model of location choice on 294 investments in the biopharmaceutical sector in 27 European countries during 2002-2006.

4.1 Investment data

The data on inward FDI comes from the Agence française des investissements internationaux (AFII, France’s agency for international investments). The database is the result of a comprehensive search by web-crawlers of public announcements of new investments from a variety of sources, including press releases, newspapers and the trade press, and Lexis-Nexis. The announcements of foreign investments are in all sectors, in Europe, between 2002 and 2006. The total number of announcements is 13 903, among which 672 investments in *biotechnology* and *drugs and cosmetics*, which are the two industry classifications we focus on. It contains information on the date of the announcement, the location of the investment (country, and sometimes city), the activity undertaken (R&D, manufacturing, distribution, administrative, etc.), the identity and country of origin of the investor, and the projected number of jobs created (in some but not all cases).

While the AFII database contains information on both new investments and expansion of existing investments, we restrict our attention to investments which represent the creation of a new facility. Investing firms may be producers of branded drugs, generic producers, medical services manufacturers, contract research organizations, and suppliers of intermediate inputs. These firms were identified by reading the text of the investment announcement, which typically contained a description of the firm’s main activity, and by looking up companies on the web. Among these we keep focus on producers of branded- drugs producers, and analyze the behavior of generic producers separately in an appendix. Our hypothesis is that only investments by research-driven pharmaceutical firms may be negatively affected by the regulatory regime, since it is primarily the profit margins of these firms that are affected by price regulation. We therefore focus on research-driven firms in our main analysis. However, we include results restricted to generic firms in an appendix as a robustness check. Finally, investments vary by the main activity. Out of a total of 294 investments, there are 78 announcements of new investments in sales offices or distribution facilities, 79 manufacturing plants, 84 new R&D facilities, 40 headquarters and administrative offices, and 8 other types of announcements (distribution centers, call centers, etc.)

Origin countries of investing firms are in all parts of the world. Destination countries are the 25 current EU members, minus Malta and Cyprus, and plus Norway, Switzerland, and the Baltic countries (Latvia, Lithuania, and Estonia), so in total 27 countries. Table (1) and Figure (1) summarize the number of investments by country. The United-Kingdom, Germany and Ireland are the three countries receiving the largest number of Bio-pharmaceutical investments over the period. These three countries receive a relatively stable number of investments each year, whereas Spain for example exhibits a sharply decreasing trend, with 12 investments in 2002,

8 in 2003, and respectively 2, 3 and 1 in the three subsequent years. Lithuania, Latvia, and Luxembourg are the three countries in which only one new facility in the Bio-pharmaceutical sector was created during 2002-2006.

4.2 Explanatory variables data

Our explanatory variables include the traditional FDI determinants and our main variable of interest, drug price regulations. Information on regulatory policies mainly come from Kyle (2007a), and was supplemented with data on a larger set of European countries and a later time period using the sources described in the appendix.

Price regulations are in the form of three dummy variables indicating whether each country uses each price policy: price control, reference pricing and therapeutic reference pricing. Table (2) and Figure (2) summarize this information. We use two additional variables explaining which countries have experienced changes in their regulatory framework during the 2002-2006 period. These are displayed in Tables (3) and (4).

The remaining explanatory variables refer to the traditional determinants of FDI used in the location choice literature. Following equation (7), we start with variables relative to local production costs: unit labor costs come from the Structural Business Statistics database from Eurostat’s Industry, Trade and Services division. Eurostat’s data are available through 2004. We extrapolate each variable forward to 2006 from 2001-2004 data.

Data on corporate taxes come from three sources. The first is the Devereux, Griffith and Klemm (2002) database, available from the IFS. This dataset omits information for the new EU members and stops in 2005. We fill in information on statutory tax rates in new EU members in 2003 and 2004 from Finkenzeller and Spengel (2004). We supplement this data with information from KPMG’s Corporate Tax Rate Survey 2006. The latter source provides information for all countries for 2005 and 2006. Data accounting for spillovers (R&D spending and the number of firms in the pharmaceutical sector for each country) are also extracted from the Eurostat database.

The construction of a market potential variable requires data on three elements: trade costs between countries r and j , consumption in pharmaceuticals in country j , and the competition index in j . Following Redding and Venables (2004), we obtain these terms by estimating gravitational trade equations. Bilateral exports from i to j can be writing as the amount exported by a representative firm from i multiplied by the number of firms in i :

$$X_{ij} = n_i p_{ij} q_{ij} = n_i c_i^{1-\sigma} \tau_{ij}^{1-\sigma} \frac{Y_j}{G_j}.$$

In logs, the latter equation writes: $\ln X_{ij} = \ln(n_i c_i^{1-\sigma}) + \ln \phi_{ij} + \ln(Y_j/G_j)$. $\phi_{ij} = \tau_{ij}^{1-\sigma}$ represents the freeness of trade between the two countries, and is specified as depending on distance, borders and language as follows: $\phi_{ij} = d_{ij}^{-\delta} e^{[-(\beta_j - \lambda L_{ij})B_{ij} + \epsilon_{ij}]}$. d_{ij} is distance between i and j , L_{ij} and B_{ij} two dummy variables taking the value 1 if countries i and j respectively share a common language or share a common border. ϵ_{ij} is an error term and β_j and λ are two parameters to estimate.

We use bilateral trade data for the years 2002-2006 in the pharmaceutical industry, and following Redding and Venables (2004) we estimate the trade equation with fixed effects for the exporting and the importing countries, respectively FX_i and FM_j . This estimation allow us to obtain a dummy per importing country, and coefficients on distance, common border and common language, with which we can build the trade costs variable. The next step is to construct the market potential variable for each country using trade costs and the importers' fixed effects: $M_r = \sum_j \phi_{ij} Y_j / G_j$. Data on common languages and on distance between countries come from CEPIL, a French research center in International Economics. Trade data come from Eurostat's structural indicators and are available online. Table (3) displays the differences in market potential across European countries, reflecting for instance the importance of Belgium as a central market, due to vicinity to large centers of demand.

5 Empirical results

We first present the results obtained from the cross-sectional price regulation dummy variables (Tables 5 and 6), and then turn to the results on the time-varying regulatory variables (Table 7).

The first column of Table (5) includes only the set of explanatory variables related to price regulation. These unconditional estimates show that overall, countries with price controls are less likely to be chosen as a destination for investment than countries without price controls. Countries with reference pricing are also less likely to receive investment, but the effect is not as strong as for price controls. Countries with therapeutic reference pricing see less investment overall than countries with generic-based regimes. And countries that combine all three systems (price controls, reference pricing, and therapeutic reference pricing) see the least investment.

In column 2, we add the market potential variable, which is positively and significantly related to the location of FDI. Controlling for market potential reduces the magnitude of the coefficient on the price control dummy, reflecting the negative correlation between these two variables, and renders the reference pricing dummy insignificant. In column 3 we add variables relating to trade costs. These are a dummy for a common language between investors and potential recipient countries, the distance between countries, and a dummy variable for Eastern

European destinations. The first and third of these are highly significant, and their inclusion renders the reference pricing and therapeutic reference pricing dummies statistically insignificant, though the price control dummy retains its negative and significant association with the probability of investment. We continue to add the elements of the profit function in columns 4-5. As expected, the nominal corporate tax rate is negatively associated with investment, while the unit cost of production has a positive coefficient (presumably reflecting variation in productivity or labor quality across locations). The latter finding is consistent with Head and Mayer (2004). When the "spillovers" variable (number of pharmaceutical establishments active in the country) is included, the market potential variable becomes insignificant, reflecting the high positive correlation between these variables. The price control dummy also becomes insignificant.³ We separate manufacturing and non-manufacturing investments in columns 6 and 7, and find that the association between regulation and investment appears to be driven by non-manufacturing investments.

The inclusion of the spillover variable is somewhat problematic. While the theory suggests an important role for inter-firm spillovers, the variable with which we measure spillovers (the number of pharmaceutical establishments in the country) makes it difficult to separately identify spillovers from other motives for investment. If the regulatory regime affects the location choices of firms, this will influence the number of establishments that previously located in the country. Thus, by controlling for the *existing* number of establishments, we are picking up the effect of the regulatory regime on the *change* in the number of establishments in the country. Since neither the price control variable nor the reference pricing variable vary within countries during our sample (they are fixed over time), it is not surprising that we find no effect of regulation on investment after controlling for the existing number of establishments. As a result, our preferred specifications for interpreting the effects of the time-invariant regulatory variables on investment will be those that exclude the spillovers variables. We will then turn to an analysis of time-varying regulatory variables, exploiting policy changes during our sample period to identify the effects of an increase in regulatory stringency on changes in investment choices. In these specifications, we will include the spillovers variables, along with country fixed effects.

Given that investment patterns may differ substantially between Western European countries and locations in Eastern Europe and the Baltic states, we present models estimated separately for these two regions in Table (6). Regulation does not appear to play a role in location

³We do not have data on the spillovers variables for Switzerland, Greece, and Lithuania, which explains why the number of observations are lower in the column that includes spillovers variables. The results associated with the other specifications are practically identical when these countries are omitted, reflecting the relatively small number of investments that take place there during this period (11 in Switzerland, 3 in Greece, and 1 in Lithuania).

decisions in Eastern Europe, while price controls are significantly associated with a 40% reduction in the odds of investment in Western European countries (as in the full sample). This distinction may reflect the types of investment taking place in these locations. Indeed, we find that when restricting to Western European countries, the regulatory variables are not significantly related to investment for manufacturing or R&D announcements, but that price controls are associated with a reduction in the odds of other types of investment. The latter types of investment include headquarters, administrative offices, sales offices, logistical and distribution centers, and services to the firm.

There are some additional interesting differences between the different types of investment. The corporate tax rate is strongly negatively associated with manufacturing investments but not the other types, while market potential is positively but insignificantly associated with manufacturing investment. This is perhaps not surprising given that production costs are likely to be the most important determinant of manufacturing locations in this industry, where transport costs are low. What is more surprising is the positive and significant coefficient on market potential for R&D investment. Common language matters for R&D and other investments, reflecting the greater importance of communication barriers in these types of investment relative to manufacturing. The distance between the country of origin and potential destination countries is not significantly related to location choices for manufacturing and R&D investments, but it increases the likelihood of other investments (at the 10% level). This may reflect the establishment of distribution centers and administrative offices associated with distant headquarters. Companies may be able to service neighboring countries from their base, but new facilities are required when expanding in more remote locations.

The specifications presented in Tables (5) and (6) are informative about the general association between price regulation and FDI in European countries. In these specifications, we have controlled for most of the key drivers of location choice. However, it is possible that there are country-specific determinants of location choice that we have omitted and that are correlated with regulatory regimes. In order to guard against this possibility, country fixed effects should be included. However, given that the price control and reference pricing dummies are constant throughout the sample period, it is impossible to measure their coefficients in a specification that includes country fixed effects. We thus exploit other policy changes that took place during the sample period (listed in Table 3). Several countries instituted therapeutic reference pricing regimes or froze prices between 2002 and 2006. The results presented in Table (7) focus on these time-varying regulatory variables, and include country fixed effects. They resemble a “difference in differences” analysis, since we control for country-specific variation in the average level of investment through the country fixed effects, and identify the additional variation in investment that takes place in countries that change their policies relative to countries that do

not change their policies.

In these specifications, we do include the spillover variables because we are interested in the change in investment relative to existing levels. We find that countries that instituted therapeutic reference pricing regimes for the first time during the period in question have a 54% lower odds of investment following the policy change than countries that did not change their policies (column 1 of Table 7). Price freezes do not appear to have any relationship with investment. When the data is broken down by type of investment, R&D investments are the only type with a significant coefficient on the therapeutic reference pricing dummy. Most of the country characteristics are insignificant after controlling for country fixed effects, with the exception of the common language dummy, which varies by investor and country and which has a strong positive association with the likelihood of investment. R&D investments are more likely to take place in countries in which more spending on R&D takes place (significant at the 10%) level, but the same is not true for manufacturing investments (in fact, R&D is negatively but insignificantly associated with investment after country effects are included).

In the appendix, we consider the relationship between price regulation and investment by generics producers. Since these firms do not have incentives to attempt to influence policy by shifting investment away of countries with more stringent price controls, we do not anticipate that the negative relationship observed between regulatory stringency and investment by research-oriented firms will be repeated. If anything, generics producers may be more likely to locate in countries that tightly regulate prices of branded drugs because these countries have greater demand for generic drugs. In appendix table (B1), we repeat our baseline regressions after restricting the dataset to generic firms. In the full sample, we find no significant relationship between regulatory policy and investment. However, when we restrict attention to investments in manufacturing facilities, we observe a positive relationship between price controls and investment (as predicted by the preceding argument about higher demand). Non-manufacturing investments (in sales and marketing, distribution, etc.) are, as expected, insignificantly related to the policy regime. Table (B2) repeats the analysis including country fixed effects, and here we observe no significant relationship between policy changes and investment.

To summarize the results discussed above, we find that foreign investors are less likely to locate new investments in countries with explicit price controls than countries with reference pricing regimes or no price regulation. However, this finding is only observed in Western European countries, and appears to be driven by investments in new sales and administrative offices. The latter result may reflect stronger incentives for investments in marketing in countries in which prices are not directly controlled, rather than a strategic action by pharmaceutical firms seeking to send a message to countries with stringent regulatory regimes. When country fixed effects are included, so that we examine the change in investment patterns associated with

changes in regulatory policy, we find that new investments significantly reduced in countries that imposed therapeutic reference pricing regimes for the first time after 2002, and that this finding appears to be driven by a reduction in R&D investments.

Why do we observe a significant impact on new R&D investments when country fixed effects are included, but not when they are omitted (Table 5 reports a coefficient on TRP that is negative but significant only at the 10% level)? One possibility is that cross-country variation in investment dominates within-country variation, and that the countries that imposed therapeutic reference pricing regimes for the first time are otherwise attractive destinations for investment. When we include fixed effects, we isolate the impact of policy changes within a country, so that our estimates are no longer confounded by cross-country variation in investment. A related possibility is that country effects control for an omitted time-invariant, country-specific variable that biased our estimates of the regulatory variables towards zero.

The finding that R&D investments are particularly affected by regulatory regimes may at first seem surprising. One might ask why, if firms seek to influence government policy by re-directing investment to countries with more favorable regulatory regimes, they do not do so with manufacturing investments. Manufacturing facilities are less closely tied to the specific science or skill base of a location, and one would expect that firms would incur lower costs in choosing a second-best location for manufacturing. However, the potential impact of locating a new R&D facility may be much greater – much more politically controversial. If governments believe that new R&D facilities contribute more to the tax base and generate greater spillovers for the region than do manufacturing facilities, they may be more sensitive to variations in the location of R&D investment. Thus the potential benefit in terms of political influence associated with the choice of an R&D location may be greater, and this may explain why the effect is mainly observed among R&D investments.

A significant limitation of these findings is that only three countries instituted therapeutic reference pricing during the sample period (Denmark, Germany, and Hungary). Spain began including patented medicine in its reference pricing system in 2007. Once investment data becomes available for 2007, we intend to incorporate it. It would be useful to extend the analysis back in time to examine earlier changes to regulatory regimes, but we do not have data that permits us to do so.

Finally, we present some comments and results as additional robustness checks. First, because these announcements are voluntary public disclosures, there is a possibility that the dataset contains a disproportionate share of large, publicly-traded firms. Since the R&D-performing pharmaceutical firms tend to be large and publicly traded, we are likely capturing a large majority of investments by these types of firms. However concerns about sample selection are likely to be more significant for smaller, privately-traded biotech firms. It is important to

keep in mind the sample composition when interpreting our results. If large, public firms are more likely to alter investment decisions in response to regulatory changes, our estimates will overstate the effect of regulation on investment by small, private firms.

Second, the data come from published sources in several languages. However, there is a possibility that because our data come from a French government agency, French-language publications may be over-represented in our database. We deal with this possibility by including in an appendix a set of estimates that exclude French-language publications. In response to a concern that investments in France or by French companies were over-represented in our data due to the origin of the dataset, we also include estimates of the models that exclude investments made in France or by French companies, and found very similar results (see the appendix).

6 Conclusions

This paper examines the relationship between cross-country differences in drug price regulation and the location of biopharmaceutical FDI in Europe. We use a theoretically-grounded location-choice model and data on 294 investments initiated in 27 European countries between 2002 and 2006 to estimate whether biopharmaceutical companies are influenced by the stringency of price regulations in choosing the countries in which to locate new investments. We find that countries with price controls receive fewer new investments, after controlling for other determinants of investment. Countries that increased the stringency of price regulation by adding patented medicines to a reference pricing regime during the sample period were approximately 50% less likely to receive an investment after the policy went into effect.

Table 1: Bio-Pharmaceutical FDI by country and year

Country	2002	2003	2004	2005	2006	Total
Austria	1	2	0	4	0	7
Belgium	1	2	6	4	1	14
Bulgaria	0	0	1	0	4	5
Switzerland	0	1	3	5	2	11
Czech Republic	1	0	1	1	1	4
Germany	7	6	4	6	11	34
Denmark	3	6	3	2	3	17
Estonia	0	0	2	0	1	3
Spain	12	8	2	3	1	26
Finland	0	1	1	1	0	3
France	5	1	3	7	2	18
UK	7	8	11	14	12	52
Greece	0	1	0	2	0	3
Hungary	3	2	1	3	1	10
Ireland	6	5	8	7	5	31
Italy	1	0	2	2	3	8
Lithuania	0	0	0	0	1	1
Luxembourg	0	0	0	1	0	1
Latvia	0	0	0	0	1	1
Netherlands	0	1	1	2	3	7
Poland	1	2	4	3	1	11
Portugal	1	0	0	3	1	5
Romania	1	0	0	0	0	1
Sweden	4	3	5	5	0	17
Slovenia	0	0	2	0	1	3
Slovakia	0	0	0	0	1	1
Total	54	49	60	75	56	294

Source: AFII database

Figure 1: Bio-pharmaceutical FDI in Europe, 2002-2006

Biopharma FDI in Europe, 2002-06

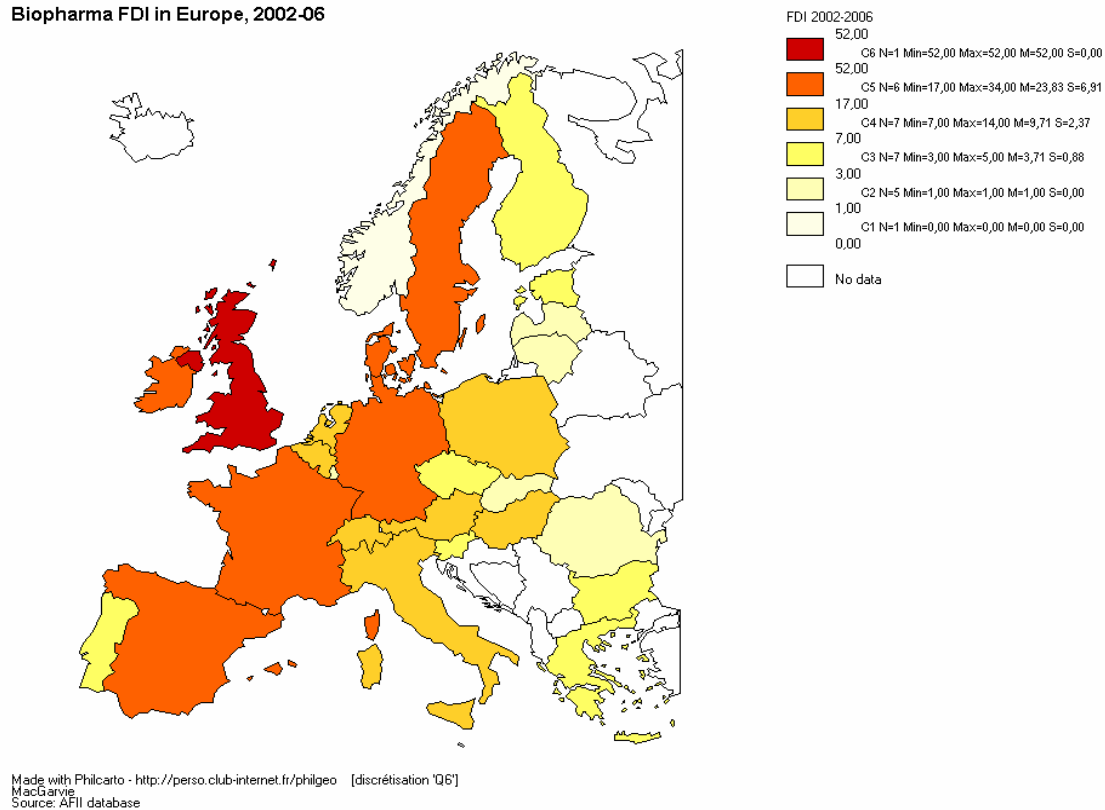
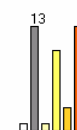
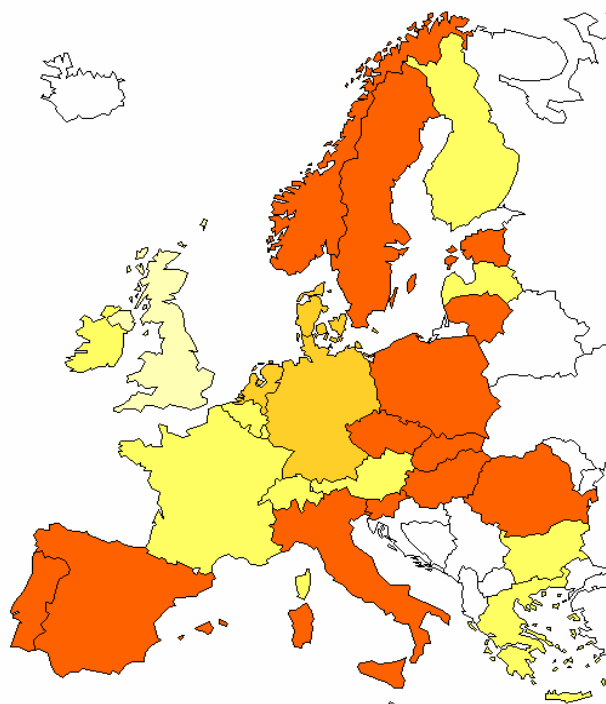


Figure 2: Price regulations in Europe

Regulatory Regimes in Europe, 2002-06



Orange: Both
RP and PC

Gold: RP only

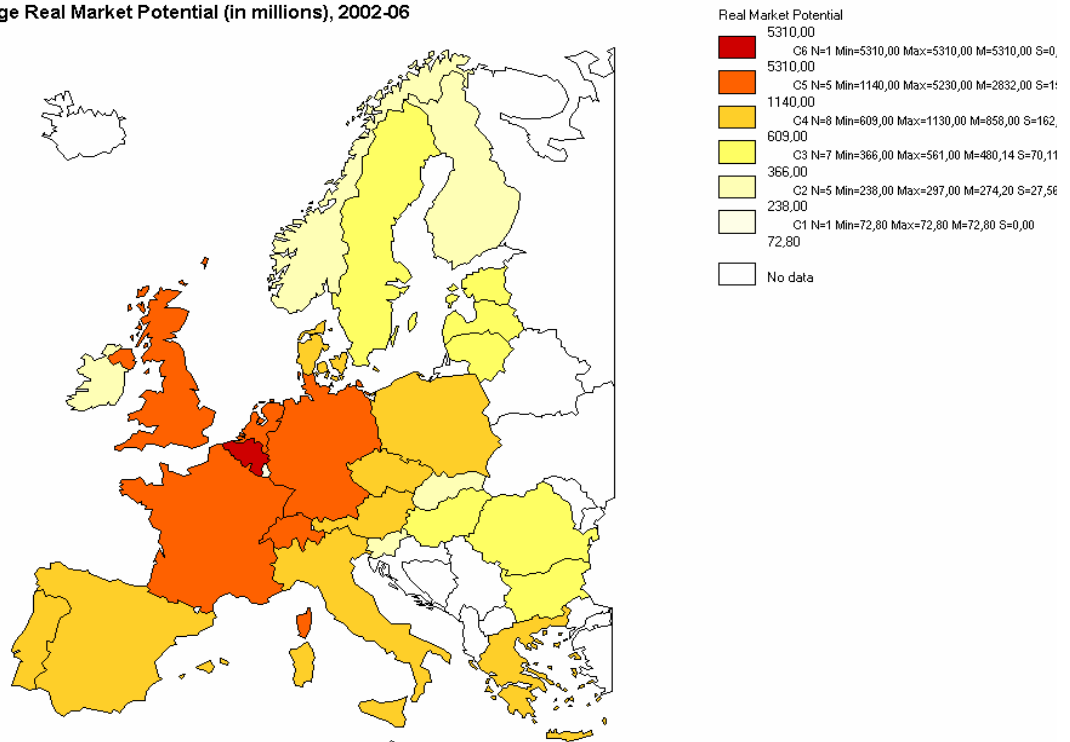
Yellow: PC only

UK: none

Made with Philcarto - <http://perso.club-internet.fr/philgeo>
MacGarvie

Figure 3: Real Market Potential in Europe

Average Real Market Potential (in millions), 2002-06



Made with Philcarto - <http://perso.club-internet.fr/philgeo> [discrétisation 'Q6']
 MacGarvie
 Source: AFII database

Table 2: Main price regulation variables

	Price control	Reference pricing	Therapeutic RP
Austria	Yes	No	No
Belgium	Yes	No	No
Bulgaria	Yes	No	No
Czech R.	Yes	Yes	Yes
Denmark	No	Yes	Starting in 2005
Estonia	Yes	Yes	No
Finland	Yes	No	No
France	Yes	No	No
Germany	No	Yes	Starting in 2004
Greece	Yes	No	No
Hungary	Yes	Yes	Starting in 2003 for statins
Ireland	Yes	No	No
Italy	Yes	Yes	No
Latvia	Yes	No	No
Lithuania	Yes	Yes	No
Luxembourg	Yes	No	No
Netherlands	No	Yes	Yes
Norway	Yes	Yes	No
Poland	Yes	Yes	No
Portugal	Yes	Yes as of 2003	No
Romania	Yes	Yes	No
Slovakia	Yes	Yes	No
Slovenia	Yes	Yes	No
Spain	Yes	Yes (except 2005-06)	starting in 2007
Sweden	Yes	Yes	No
Switzerland	Yes	No	No
UK	No	No	No

Source:see data appendix

Table 3: Price cuts and freezes, 2002-2006

Country	Date	Description
Germany	Oct-03	16% reduction in reimbursed prices for patented medicines.
Hungary	Apr-04	government froze retail drug prices at 85% of their previous levels for 180 days.
Hungary	Jun-04	Parliament passed an amendment to the Price Act allowing the government to freeze drug prices for up to nine months.
UK	Nov-04	7% cut in prescription drug prices after negotiations with the Association of the British Pharmaceutical Industry (ABPI).
Spain	March 2005, March 2006	The Ministry of Health imposed a compulsory 4.2% price cut from March 2005 and a 2% price cut from March 2006 for all products not subject to reference prices and with a price higher than EUR2.
Italy	Approved June 1, effective October 1, 2006	The Italian Drug Agency (AIFA) imposed a temporary 5% cut on the price of drugs used by the country's National Health Service (SSN)
		Poland Jul-06 13% price cut for imported products

Table 4: Changes to Reference Pricing Programs, 2002-2006

Country	Date	Description
Portugal	2003	Adopted reference pricing scheme in which amount reimbursed depends on the price of the least expensive equivalent generic drug available
Hungary	2003	Therapeutic reference pricing for statins
Spain	2004	Reference pricing suspended; price cuts used to compensate
Germany	2004	Included patented medicines in reference pricing scheme
Denmark	2005	Reference pricing scheme shifts from comparisons with cheapest generic drug to comparisons with other European countries.
Spain	2007	Therapeutic reference pricing scheme goes into effect

Table 5: Baseline results including all countries, types of investment, and investors

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	Full Sample					Manufacturing	Non-manufacturing
price controls	-1.521 (0.136)***	-0.880 (0.179)***	-0.570 (0.187)***	-0.452 (0.191)**	-0.286 (0.214)	-0.018 (0.410)	-0.598 (0.220)***
reference pricing	-0.388 (0.133)***	-0.153 (0.144)	0.249 (0.155)	0.321 (0.178)*	0.313 (0.180)*	-0.083 (0.320)	0.529 (0.218)**
Therapeutic RP	-0.503 (0.199)**	-0.568 (0.201)***	-0.348 (0.214)	-0.329 (0.212)	-0.378 (0.218)*	0.450 (0.419)	-0.666 (0.249)***
ln market potential		0.396 (0.077)***	0.272 (0.074)***	0.393 (0.104)***	0.130 (0.123)	0.213 (0.199)	0.450 (0.125)***
ln distance			0.136 (0.168)	0.233 (0.182)	0.092 (0.190)	0.260 (0.341)	0.158 (0.216)
common language			1.159 (0.178)***	0.903 (0.183)***	0.892 (0.191)***	0.654 (0.349)*	0.995 (0.216)***
Eastern Europe			-0.929 (0.214)***	-0.561 (0.310)*	-0.224 (0.350)	-0.515 (0.557)	-0.600 (0.386)
ln unit costs				0.511 (0.167)***	0.124 (0.265)	0.562 (0.296)*	0.450 (0.206)**
ln corporate tax rate				-1.103 (0.298)***	-1.481 (0.319)***	-1.656 (0.461)***	-0.638 (0.398)
ln # firms					0.391 (0.102)***		
ln rd expenditure					0.215 (0.087)**		
Combined effects of price regulation variables, expressed as odds ratios:							
RP + TRP	0.410***	0.486***	0.906	0.993	0.937	1.443	0.872
Observations	7938	7938	7938	7250	6448	1975	5275
Log Likelihood	-909.669	-896.272	-863.446	-824.447	-745.392	-229.344	-581.002
PseudoR2	0.061	0.075	0.109	0.117	0.147	0.098	0.145

Source: Standard errors in parentheses * significant at 10%, ** significant at 5%; *** significant at 1%

Table 6: Comparing Across Types of Investment

	Dependent variable: location choice dummy				
	Estimation method: conditional logit				
	(1) Eastern Europe	(2) Western Europe	(3) W. Europe, Manufacturing	(4) W. Europe, R&D	(5) W. Europe, Other
price controls	-0.485 (0.610)	0.426 (0.201)**	-0.025 (0.374)	0.591 (0.403)	0.651 (0.303)**
reference pricing	1.022 (0.653)	-0.528 (0.238)**	0.169 (0.522)	-0.925 (0.483)*	-0.838 (0.337)**
Therapeutic RP	-0.417 (0.953)	-1.184 (0.339)***	-1.864 (0.539)***	-1.017 (0.709)	-0.280 (0.604)
corporate tax rate	-0.343 (0.697)	0.424 (0.115)***	0.276 (0.221)	0.612 (0.225)***	0.369 (0.175)**
ln market potential	-0.695 (0.478)	0.387 (0.205)*	0.174 (0.375)	0.285 (0.374)	0.557 (0.321)*
ln distance	0.199 (0.322)	0.545 (0.227)**	0.479 (0.427)	0.897 (0.491)*	0.294 (0.340)
ln unit costs		-0.496 (0.204)**	-0.084 (0.449)	-0.336 (0.363)	-0.879 (0.307)***
common language		0.938 (0.190)***	0.583 (0.365)	1.187 (0.347)***	0.977 (0.294)***
RP+TRP		0.903	1.155	0.716	0.829
Observations	261	4176	1072	1168	1936
Log Likelihood	-59.493	-665.028	-169.625	-175.721	-303.509
PseudoR2	0.066	0.081	0.087	0.132	0.095

Standard errors in parentheses, * significant at 10%, ** significant at 5%, *** significant at 1%

Table 7: Impacts of Policy Changes

	Dependent variable: location choice dummy Estimation method: conditional logit					
	Country fixed effects included					
	(1)	(2)	(3)	(4)	(5)	(6)
	Full sample					
				Manufacturing	R&D	Other
Therapeutic RP	-0.772 (0.372)**		-0.696 (0.376)*	0.121 (0.748)	-1.979 (0.880)**	-0.823 (0.540)
Price Freeze		-0.327 (0.257)	-0.229 (0.262)	-0.639 (0.616)	0.034 (0.523)	-0.101 (0.390)
corporate tax rate	-0.001 (1.150)	0.341 (1.144)	0.077 (1.156)	2.229 (1.860)	-3.416 (2.771)	-2.114 (2.425)
Common language	0.908 (0.200)***	0.912 (0.199)***	0.912 (0.200)***	0.646 (0.372)*	1.012 (0.360)***	1.128 (0.328)***
ln market potential	0.319 (0.308)	0.099 (0.316)	0.234 (0.323)	-0.167 (0.628)	0.518 (0.623)	0.490 (0.526)
ln R&D expenditure	-0.007 (0.250)	-0.127 (0.241)	-0.042 (0.250)	-0.165 (0.411)	1.186 (0.684)*	-0.128 (0.484)
ln distance	0.011 (0.191)	0.023 (0.191)	0.010 (0.191)	0.068 (0.368)	-0.033 (0.354)	-0.032 (0.292)
Ln unit cost	-0.786 (0.944)	-0.884 (0.903)	-0.730 (0.928)	-0.243 (1.482)	2.552 (2.929)	-1.301 (1.799)
ln # firms	1.390 (0.610)**	1.207 (0.611)**	1.478 (0.616)**	1.722 (1.219)	1.055 (1.185)	1.758 (1.055)*
TRP + Freeze(odds ratio)			0.397**	0.595	0.142**	0.397
Observations	6448	6448	6448	1746	1904	2798
Log Likelihood	-721.209	-722.574	-720.825	-190.488	-190.443	-293.316
Pseudo R2	0.175	0.173	0.175	0.193	0.261	0.228

Standard errors in parentheses,* significant at 10%; ** significant at 5%; *** significant at 1%

Table 8: Robustness Checks Excluding French Investments

	Dependent variable: location choice dummy							
	Estimation method: conditional logit							
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Excluding French-language publications		Excluding France as destination or origin		Country FEs		non-mfg	
	Country FEs		non-mfg		Mfg		mfg	
price regulation	0.657 (0.151)*		0.658 (0.169)	0.616 (0.321)	0.751 (0.172)		0.666 (0.173)	1.188 (0.581)
reference price	1.322 (0.245)		1.594 (0.359)**	0.977 (0.331)	1.358 (0.293)		1.699 (0.453)**	0.916 (0.364)
Therapeutic RP	0.670 (0.152)*	0.464 (0.183)*	0.526 (0.140)**	1.100 (0.499)	0.614 (0.146)**	0.452 (0.185)*	0.521 (0.143)**	0.720 (0.372)
freeze		0.812 (0.221)				0.637 (0.183)		
ln market potential	0.984 (0.130)	1.324 (0.438)	1.144 (0.171)	0.630 (0.185)	1.188 (0.160)	1.468 (0.535)	1.372 (0.218)**	0.847 (0.228)
common language	2.672 (0.535)***	2.754 (0.584)***	2.810 (0.667)***	2.557 (0.980)**	2.455 (0.511)***	2.487 (0.540)***	2.562 (0.639)***	2.331 (0.923)**
ln distance	1.035 (0.202)	0.961 (0.188)	0.951 (0.219)	1.143 (0.424)	1.054 (0.212)	0.960 (0.189)	1.052 (0.251)	0.944 (0.359)
corporate tax rate	0.267 (0.088)***	1.313 (1.584)	0.398 (0.173)**	0.182 (0.096)***	0.249 (0.086)***	1.811 (2.230)	0.320 (0.146)**	0.216 (0.120)***
ln unit cost	0.958 (0.269)	0.410 (0.412)	0.960 (0.321)	0.806 (0.418)	1.060 (0.292)	0.223 (0.248)	1.110 (0.362)	0.756 (0.406)
E. Europe	0.674 (0.252)		0.667 (0.307)	0.656 (0.453)	0.627 (0.238)		0.604 (0.279)	0.741 (0.537)
ln # firms	1.498 (0.163)***	5.684 (3.655)***	1.405 (0.174)***	1.654 (0.382)**	1.383 (0.159)***	7.140 (4.806)***	1.340 (0.178)**	1.328 (0.307)
ln rd expenditure	1.288 (0.121)***	0.997 (0.258)	1.274 (0.136)**	1.376 (0.267)*	1.223 (0.106)**	0.892 (0.244)	1.177 (0.112)*	1.499 (0.306)**
Observations	6029	6029	4399	1630	5260	5260	3878	1382
Log Likelihood	-692.433	-668.813	-495.207	-185.589	-617.405	-591.735	-443.819	-161.358
Pseudo R2	0.153	0.182	0.170	0.158	0.160	0.195	0.181	0.162

Standard errors in parentheses, * significant at 10%; ** significant at 5%; *** significant at 1%

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Appendix A: Drug price regulation data

Information on regulatory policies by country come from a variety of sources. The starting point was Table 2 of Kyle (2007a). This was supplemented with information on a larger set of European countries and a later time period using the following sources:

Kalo, K, N. Muszbek, J. Bodrogi and J. Bidlo, (2007), “Does therapeutic reference pricing always result in cost-containment? The Hungarian evidence”, *Health Policy*, Volume 80, Issue 3, March 2007, Pages 402-412

Patricia Danzon and Jonathan Ketcham, (2003) “Reference pricing of pharmaceuticals for Medicare: Evidence from Germany, The Netherlands and New Zealand”, National Bureau of Economic Research, working paper 10007

Mossiolo, P. et al (eds.) (2004) *Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality*, Open University Press.

Kuszevski K, Gericke C. (2004) *Health Systems in Transition: Poland*. Copenhagen, WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies.

Karaskevica, J. and E. Tragakes (2001) *Health Systems in Transition: Latvia*. Copenhagen, WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies.

Jesse M, Habicht J, Aaviksoo A, Koppel A, Irs A, Thomson S. (2004) *Health care systems in transition: Estonia*. Copenhagen, WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies.

Vladescu, C., S. Radulescu, and V. Olsavsky (2000) *Health care systems in transition: Romania*. Copenhagen, WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies.

Huttin, M. (1999), “Drug Price Divergence in Europe: Regulatory Aspects” *Health Affairs*, Volume 18, number 3, May/June 1999.

Pharmaceutical Research and Manufacturers of America (2007), *National Trade Estimate Report on Foreign Trade Barriers (NTE)*.

Office of the U.S. Trade Representative (2005), *2005 National Trade Estimate Report on Foreign Trade Barriers*

Appendix B: Tables on generics producers

Table B-1: Results restricted to generics producers including all countries, types of investment, and investors

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
			Full Sample			Mfg	Non-Mfg
price regulation	-0.252 (0.307)	0.508 (0.367)	0.675 (0.384)*	0.567 (0.392)	0.220 (0.458)	1.523 (0.676)**	-0.084 (0.542)
reference price	0.163 (0.228)	0.399 (0.245)	0.551 (0.252)**	0.319 (0.269)	0.211 (0.281)	1.098 (0.430)**	-0.167 (0.379)
Therapeutic RP	-0.073 (0.344)	-0.156 (0.348)	0.066 (0.382)	0.040 (0.392)	-0.022 (0.404)	0.277 (0.528)	-0.127 (0.632)
ln market potential		0.502 (0.136)***	0.381 (0.140)***	0.231 (0.172)	-0.140 (0.250)	0.308 (0.285)	0.133 (0.236)
ln distance			-0.019 (0.253)	0.039 (0.266)	-0.174 (0.292)	-0.432 (0.334)	0.562 (0.444)
common language			0.553 (0.378)	0.475 (0.395)	0.010 (0.451)	0.632 (0.587)	0.365 (0.556)
EE			-0.562 (0.305)*	-0.378 (0.494)	0.149 (0.570)	-0.333 (0.665)	-1.872 (1.243)
ln unit cost				-0.012 (0.242)	0.128 (0.359)	-0.225 (0.302)	0.324 (0.505)
corporate tax rate				0.882 (0.584)	-0.165 (0.624)	0.011 (0.697)	1.604 (1.079)
ln # firms				0.737 (0.184)***			
ln rd expenditure				-0.044 (0.092)			
Observations	2511	2511	2511	2300	1926	1125	1175
Log Likelihood	-305.837	-298.990	-295.968	-285.760	-241.850	-137.270	-129.311
Pseudo R2	0.002	0.025	0.034	0.035	0.073	0.052	0.145

Source: Standard errors in parentheses; * significant at 10%; ** significant at 5%; *** significant at 1%.

Table B-2: Results restricted to generics producers, including country fixed effects

	(1)	(2)	(3)	(4)	(5)
	Full Sample			Mfg	Non-Mfg
Therapeutic RP	0.579 (0.757)		0.534 (0.782)	-0.120 (1.179)	0.722 (1.254)
freeze		0.211 (0.479)	0.125 (0.502)	0.554 (0.842)	0.294 (0.703)
corporate tax rate	1.457 (1.600)	1.462 (1.605)	1.418 (1.607)	2.470 (2.142)	-3.610 (4.429)
common language	0.180 (0.462)	0.188 (0.462)	0.183 (0.462)	0.738 (0.651)	-0.355 (0.775)
ln market potential	0.344 (0.570)	0.484 (0.593)	0.396 (0.609)	1.817 (1.044)*	0.130 (0.847)
ln rd expenditure	0.075 (0.261)	0.071 (0.262)	0.079 (0.261)	0.130 (0.312)	0.684 (1.132)
ln distance	-0.239 (0.295)	-0.231 (0.293)	-0.236 (0.294)	-0.775 (0.380)**	0.679 (0.555)
ln unit cost	-1.251 (1.378)	-1.131 (1.362)	-1.243 (1.379)	-1.477 (1.566)	-2.484 (3.805)
ln # firms	-0.895 (0.996)	-0.718 (0.966)	-0.866 (1.008)	-1.773 (1.790)	-2.004 (1.575)
Observations	1926	1926	1926	1002	924
Log Likelihood	-224.821	-225.029	-224.790	-105.242	-93.529
PseudoR2	0.139	0.138	0.139	0.223	0.255

Source: Standard errors in parentheses; * significant at 10%; ** significant at 5%;

*** significant at 1%